

Development of an hES Cell-Based Assay System for Hepatocyte Differentiation Studies and Predictive Toxicology Drug Screening

Grant Award Details

Development of an hES Cell-Based Assay System for Hepatocyte Differentiation Studies and Predictive Toxicology Drug Screening

Grant Type: Tools and Technologies I

Grant Number: RT1-01012

Investigator:

Name:	Kristina Bonham
Institution:	VistaGen Therapeutics, Inc.
Type:	PI

Disease Focus: Liver Disease, Metabolic Disorders, Toxicity

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$971,558

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: NCE

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Grant Application Details

Application Title: Development of an hES Cell-Based Assay System for Hepatocyte Differentiation Studies and Predictive Toxicology Drug Screening

Public Abstract:

Drug-induced liver toxicity, including that from FDA-approved drugs, is the leading cause of liver failure in the US. One of the biggest road blocks to testing drug-induced liver toxicity prior to clinical studies or release of the drug into the market is the absence of a good model of human drug metabolism in the liver. Development of a clinically predictive drug screening system would allow earlier detection of drug-induced liver toxicity, thus decreasing drug costs, decreasing the scale of pre-clinical animal testing, and increasing drug safety. Unfortunately, use of primary human liver cells for drug screening is hampered by their limited availability and poor viability in culture. Human embryonic stem (hES) cells, however, could provide a renewable, scalable, relevant source of liver cells since they can be induced to turn into these types of cells. Unfortunately, though, current hES protocols yield primarily immature liver cells, even though mature adult-like liver cells would be needed for drug screening. Here we propose development of a new hES cell line tool that attaches a fluorescent molecule to a protein found in mature liver cells. This would be a very powerful tool for two key avenues of study and development. First, it will facilitate testing of new methods to enhance the maturation of hES-derived liver cells, ultimately leading to better protocols for transplantation and regenerative medicine purposes. Second, it will also be instrumental in screening for drug-induced liver toxicity effects. While [REDACTED] interests lie more with the usage of this tool for drug screening purposes, we plan to openly share this tool with the scientific community under standard licensing agreements so that rapid progress can be made in both these areas.

Statement of Benefit to California:

This proposal has been submitted by a California company whose mission is to develop and commercialize ES cell-based assays to aid in drug discovery and development. Using stem cells to model how the liver metabolizes drugs would lead to earlier detection of drug-induced liver toxicity, keeping many of the more dangerous clinical drugs from ever reaching the market. This would increase drug safety, decrease drug costs, and decrease the scale of pre-clinical animal testing that is currently used in drug development benefiting all Californians.

The work outlined in this proposal will also bring significant revenue into California, in various different forms. Whenever possible, we will continue to order supplies and/or use services through our standing relationships with California vendors, such as E&K Scientific (Santa Clara, CA), Invitrogen (Carlsbad, CA), and Stanford University Core Research facilities in order to support California businesses and universities. Partnering and licensing of the technology developed in this proposal, as well as commercialization of new and safer drugs, would bring revenue and additional jobs into California. In addition, patents arising from these technologies are also potentially significant for California, due to the licensing revenue fees that would go back to the state.

The ES cell line tool generated as a result of this proposal, along with the reagents used to make it, will be shared openly with the scientific community under transfer and/or licensing agreements that are standard to both academic and industrial scientific entities. This will facilitate rapid progress toward two key avenues of research and development: 1) screening drugs for potential toxic effects on the liver and 2) for better understanding liver development, ultimately leading to better protocols for transplanting ES-derived liver cells into patients with liver disease or drug-induced liver toxicity. This would also result in more jobs in California to carry out this work and would form the basis of additional academic and corporate collaborations that would increase California's leadership role in stem cell applications.

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